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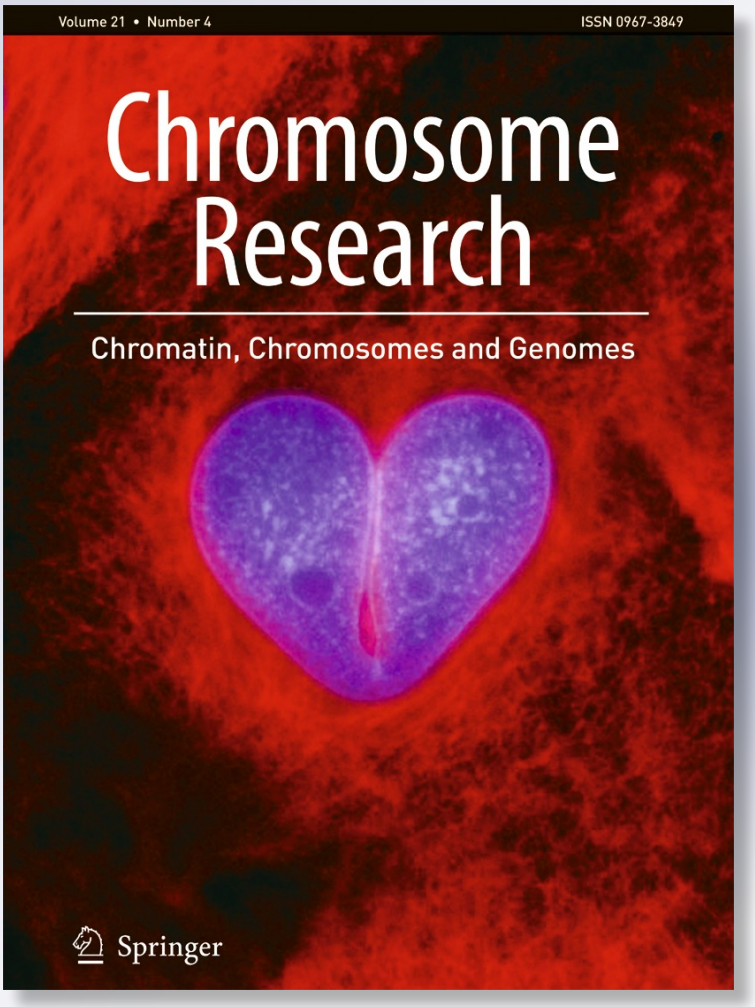

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A remarkable career in science—Joseph G. Gall

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Abstract A festive group of ~150 current and former students, postdoctoral and other associates, and colleagues gathered during the weekend of April 12–14, 2013 to celebrate Joe Gall's 85th birthday. The gathering, hosted by the Carnegie Institution for Science, Department of Embryology (Allan Spradling, Director) and organized by a group of Joe's current and former students (Zehra Nizami, Alison Singer, Ji-Long Liu, Virginia Zakian, Susan Gerbi), was held in Baltimore, MD. Dinners and symposia extending over 3 days celebrated Joe's scientific findings over the years, together with those of his former students, postdoctoral fellows, and other associates (see program at https://sites.google.com/site/gallsymposium2013/).

Keywords Lampbrush chromosomes · Amphibian oocytes · Extrachromosomal rDNA · In situ hybridization · sisRNA

Abbreviation
sisRNA Stable intronic sequence RNA

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Joe Gall's scientific career has spanned nearly 70 years—from 1942, when he received his first microscope as a gift from his parents and began using it to study natural specimens collected on his parents' farm, to the present, where he continues to make important discoveries about cells, the organization of molecules in the cell, and how they function. Much of Joe's interests over the years have focused on chromosomes and their structure, the organization of DNA in the nucleus, changes in gene number in oocytes and other cells, transcription of RNAs, and the cellular complexes involved in RNA processing. His findings have touched on many basic problems in chromosome structure and function, including the number of DNA strands per chromatid, the nature of chromosomal ends, and how chromosomal DNA is replicated. They have also focused on gene structure and function—the nature of a transcription unit in eukaryotic cells and the processing of nascent RNA.

Throughout his career, a hallmark of Joe's work has been a deep interest in biology and the natural history of organisms, coupled with the use of diverse organisms to investigate specific biological problems. For example, the giant lampbrush chromosomes of amphibians provided material that inspired his early experiments, while the ciliated protozoan *Tetrahymena* with its extrachromosomal rDNA and abundance of short macronuclear DNA fragments was an ideal organism for studying the structure and replication of extrachromosomal rDNA, and for discovering the molecular nature of chromosome ends, or telomeres. Work in his lab revealed that telomeres contain hexanucleotide repeats (Blackburn and Gall 1978), providing the foundation for the Nobel prize winning discovery of telomerase by his former postdoctoral student Elizabeth Blackburn and her student Carol

Greider. By selecting an organism appropriate to the biological problem under consideration, Joe has made important findings that are of general significance and relevant to many eukaryotic organisms. More than this, however, the qualities that define Joe's science have been a deep interest in the problem in which he is engaged, the insight to formulate a sometimes deceptively simple experiment to address the problem, and a clear and thoughtful interpretation of the findings.

Joe's scientific contributions have had major impacts on the way we think about chromosomal DNA and gene structure, and the changes in DNA that occur during development, as well as RNA and its processing in the cell. His many scientific findings (Endow and Gerbi 2003) have been recognized by the scientific community by a number of awards that, during the past decade, include the 2006 Albert Lasker Award for Special Achievement in Medical Science and 2007 Louisa Gross Horwitz Prize. Joe has also contributed to the scientific community: he served as President of the American Society for Cell Biology (ASCB) in 1968 and received the 1983 E.B. Wilson Medal, the ASCB'S highest honor for science. He also served as President of the Society for Developmental Biology (SDB) in 1985 and was awarded the 2004 SDB Lifetime Achievement Award.

Joe's impact as a scientist is further reflected in the large number of PhD thesis students he has trained throughout his career (>30), as well as the numerous postdoctoral fellows (>40) and other laboratory members he has mentored. He has played a pioneering role in efforts to help women gain equal stature in the scientific community, which is reflected in the extraordinary outcome that three of his former women mentees (Mary-Lou Pardue, Susan Gerbi, Elizabeth Blackburn) have been elected ASCB President during their careers. In recognition of his superlative training record, he received the 1996 AAAS Lifetime Mentor Award and the 2006 ASCB Women in Cell Biology Lifetime Achievement Award. He is also a member of the Rosalind Franklin Society, whose mission is to promote the contributions of women in the life sciences.

It could be said that Joe never misses a teaching opportunity, not only participating in formal settings, such as the popular microscopy course he taught during his time at Yale University and now teaches at the Carnegie Institution, but also by taking time to point out an interesting insect species on a walk or demonstrating how to observe a solar eclipse safely. In addition, his daily habits endear him to his colleagues; he is a regular lunchroom companion and his office door is always open to those brandishing a freshly developed Northern blot, seeking advice, or requiring taxonomic identification of a freshly captured "critter." His accessibility and unhurried disposition are testaments to his reasoned approach to science, his disciplined work schedule, and exceptional organizational skills. The photograph shows Joe seated at the dissecting microscope on his lab bench, where visitors to the laboratory will typically find Joe hard at work on his latest experiments.

The birthday symposium began with a plenary talk by Joe, focusing on key events and findings during his career, including his parents' move to a farm during WWII and the impact of the rural environment on his interest in nature (Gall 2006). Lampbrush chromosomes, the object of Joe's PhD thesis research more than 60 years ago, resurfaced at several times during his career and still play a prominent part in his work on chromosomes (Kaufmann et al. 2012; Liu and Gall 2012). His visualization by phase contrast microscopy of the kinetics of breakage of the lampbrush chromosome loops by DNAse provided early evidence that a chromosome contains a single double helix of DNA (Gall 1963). Joe used amphibian oocyte nuclei with their cap of amplified ribosomal DNA to develop the now widely used method of in situ hybridization (Gall and Pardue 1969). After decades of research with a variety of organisms, including *Drosophila*, *Tetrahymena*, and *Dytiscus*, and study of many nuclear organelles

including the Cajal Body, Joe has returned to studying the amphibian oocyte where his "deep" sequencing of lampbrush chromosome RNA has revealed stable intronic sequences (Gardner et al. 2012).

The meeting continued with presentations by Joe's many former students, postdocs, and other associates. Talks on RNA included viral noncoding RNPs (Joan Steitz) (Steitz et al. 2011), identification of rRNA conserved nucleotide elements that highlight functional sites in ribosomes (Susan Gerbi, in preparation), analysis of the phosphoprotein P0 ribosomal stalk protein and its intriguing nonribosomal function in *Plasmodium* where it is located on the cell surface (Linda Hufnagel, unpublished), *RNAi* knock-down of *Nopp140* RNA that results in cytoplasmic particles of decapping protein as part of the nucleolar stress response (Patrick DiMario) (James et al. 2013), in vivo tracking by GFP of *nanos* and *oskar* RNAs that localize at the posterior pole of *Drosophila* embryos (Liz Gavis) (Lerit and Gavis 2011), and RNA editing (Michael Jantsch) (Levanon et al. 2005). A session on developmental biology included development of the vertebrate eye (Rob Grainger) (Jin et al. 2012) and the role of the *Rax* gene (Milan Jamrich) (Bailey et al. 2004), heparin sulfate proteoglycan synthesis that allows generation of the BMP gradient in *Drosophila* embryos (Rahul Warrior) (Bornemann et al. 2008), dorsal appendage formation in *Drosophila* (Celeste Berg) (Dorman et al. 2004), and the role of SOX9 in gonad development (May Penrad-Mobayed) (El Jamil et al. 2008). A cell biology session included the molecular mechanism of force production in spindles by a kinesin motor (Sharyn Endow) (Liu et al. 2012), design and expression of affinity reagents for research by fusing the protein of interest to the M13 coat protein (Brian Kay) (Huang et al. 2012), the cytoophidium/CTP synthase compartment (Ji-Long Liu) (Liu 2010), study of a mouse model for Rett syndrome whose phenotype can be reversed by expression of the *MeCP2* gene (Adrian Bird) (Bird 2011), and treatment of acute myeloid leukemia (Harry Erba) (Levis et al. 2011).

A session on model organisms included a study of *Hydra* regeneration by *RNAi* against targets identified in a chemical genetics screen (Rob Steele) (Chapman et al. 2010), requirement of *AS12* transcription for endocycling in *Tetrahymena* (Kathy Karrer) (Yin et al. 2010), and T cell response by catfish to a parasitic ciliate (Craig Findly, unpublished). A session on chromosomes touched on maintenance of *Drosophila* telomeres and centromeres (Mary-Lou Pardue) (Pardue and DeBaryshe 2011), gene conversion and hypomethylation in *Coprinus* (Pat Pukkila) (Stajich et al. 2010), splicing factor recruitment to lampbrush chromosomes (Michel Bellini) (Kim et al. 2012), evolution of H3K4 methyltransferases (Manuel Diaz) (Chauhan et al. 2012), and Pif1 helicases that can overcome replication fork barriers such as those caused by G-quadruplex DNA (Virginia Zakian) (Paeschke et al. 2013).

A talk by current members of the Gall lab highlighted recent findings and illustrated how Joe continues to steer the lab in new directions by applying sophisticated technologies to classical problems. Zehra Nizami introduced the lab's latest discovery of a novel class of noncoding RNA derived from the introns of transcribed genes, termed stable intronic sequence RNA (sisRNA) (Gardner et al. 2012). These RNAs were identified by performing next-generation sequencing on pure nuclear versus cytoplasmic fractions of the cell, which Joe obtained by hand-isolating germinal vesicles from giant amphibian oocytes. Eugene Gardner described the initial characterization of nuclear sisRNA, and Gaëlle Talhouarne talked about sisRNA that occurs in the cytoplasm. The lab is currently attempting to understand the function of sisRNA by using a genetic model system. To this end, Jun Wei Pek showed preliminary data on sisRNA in *Drosophila*.

The scientific sessions included an animated discussion on the function of journals and open access publishing policies, led by Korie Handwerger (Cell Press/Elsevier), who presented the "article of the future" format, exemplified by a recent paper from Joan Steitz's laboratory (Tycowski et al. 2012). Issues raised by audience members include the reluctance of journals to publish work that confirms previous findings, the obligation of journals to admit errors in publishing papers and highlight them, and the question of the usefulness of open access to second and third world countries, including sub-Saharan African populations, where Internet infrastructure and stability are the limiting problems to dissemination of scientific findings, rather than immediate access to journal articles.

Well-attended informal talks included those by Joe's wife Diane Dwyer, son Larry, and daughter Barb on life with Joe, comments by his colleagues at the Carnegie Institution (Don Brown, Marnie Halpern), and poignant remarks by Allan Spradling regarding Joe's impact on his own science through his deep interest in biology and

his appreciation of good science. Former colleagues at the meeting (Joel Rosenbaum, Steve McKnight) praised Joe as a scientist and person, and others honored Joe by their presence (Giuseppina Barsacchi, Ed Cohen, Nanni Din, Marty Gorovsky, Nancy Lane, Kathy Mahon, Tony Mahowald, Liz Rogers, Ed Stephenson, Martha Truett, Karen Vavra). Finally, an evening session led by Adrian Bird allowed former lab members to relate anecdotes and remarks regarding their time with Joe that were variously amusing, insightful, and moving.

Attendees came from 8 countries and 16 states to attend the meeting, a remarkable testimony to Joe's long-reaching personal scientific influence. As Don Brown (*Director Emeritus*, Carnegie Institution) pointed out, most scientists reach their peak and are well into career decline by their 70s—Joe is highly unusual in that he has continued to maintain his scientific productivity and insight well into his ninth decade. All of us attending the symposium look forward to the next Joe Gall Symposium, which has been held at intervals of 10 or 20 years for the past 40 years, and hope that we will be there to follow Joe's remarkable example of noteworthy science and admirable health.

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